A COMPREHENSION STUDY ON REGULATION OF HERBAL DRUGS IN USA, EUROPEAN UNION AND INDIA

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REVIEW ARTICLE

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DOI: https://doi.org/10.22270/ijdra.v5i4.205

ABSTRACT

The present study reviews the regulations of herbal drugs in the EU, US and India and throws light upon issues related to their clinical trials. Herbal drugs have been used for a long time in different systems of health like *Ayurveda, Yunani, Sidha* and Homeopathy for treating number of diseases. It is a very difficult to perform clinical study on herbal drugs because these drugs are a complex combination of active ingredients. It is therefore difficult to identify the ingredient which is responsible for the therapeutic effect amongst various ingredients of herbal drugs. The standardization of herbal drugs is also a very difficult task. In spite of all these problems are existing public interest has increased towards herbal drugs in last 2-3 decades because of their long history of treating the disease safely. The laws and regulations for herbal drugs are different in different countries. The WHO has stated that each country should have a system to regulate herbal drugs in their territory. In the EU the committee on herbal medicinal products (HMPC) which part of the EMA was established under regulation (EC) No. 726/2004 and European directive 2004/24/EC in September, 2004. The main duty of HMPC is to evaluate and give authorization for herbal drugs on the basis of their safety and efficacy. In US herbs are classified as dietary supplements after the introduction of the Dietary Supplement Health and Education Act (DSHEA) in1994. In US herbal drugs are categorized into two types, first is OTC herbal drugs and drugs which required NDA approval. In India the Department of AYUSH has made guidelines for quality enhancement of herbal substances. The present study reviews the regulations of herbal drugs in the EU, US and India and throws light upon issues related to their clinical trials.

Keywords: AYUSH, Ayurveda, FDA, CDSCO, Regulation, Clinical trials, Herbal drugs.

INTRODUCTION

Herbal medicines are defined by the World Health Organization (WHO) as "the aerial or underground plant parts or other plant material that contain an active ingredient as finished labeled medicinal product." World Health Organization reported that traditional medicines are used by about 80% of the world population for their primary health care treatments. The long history of herbal medicines describes that these are being used for a long time with better patient tolerance. Those countries which have better agro culture condition can provide herbal medicine easily on cheaper rates. (1) Public interest towards natural therapy called as herbal medicines has been increased not only in developing countries, but also in developed countries in the past 2-3 decades. In 1990, expenditure associated with "alternative" therapy in the United States was estimated to be US$13.7 billion. This had doubled by the year 1997, with herbal medicines growing faster than any other alternative therapy. (2) In Australia, Canada, and the United Kingdom, annual expenditure on traditional medicine is estimated to be US$80 million, US$1 billion, and US$2.3 billion, respectively. Some of the important factors responsible for the worldwide growth of the herbal medicine market are mentioned below (3):

1. Natural therapy has emerged as an alternative to synthetic medicines to a large extent worldwide.
2. Belief of health professionals that herbal medicines have lower adverse effects in comparison to modern medicines.

3. Some conventional therapies, where treatment paradigm is quite slow, psychologically patient finds solace in herbals.

4. Many people have a longing of self-medication.

5. Increase in number of herbal medicines with improved quality, efficacy and safety.

6. People who are dissatisfied with limited result of synthetic medicines as this medicine primarily treating the symptoms like chronic pain associated with conditions such as cancer later shows belief in herbal medicines

7. Increase in research in herbs has given scientific evidences in support of their use as medicines.

8. Many herbal drugs like caraway ginger. Turmeric etc. which are otherwise used as food are ingredients of herbal medicine formulations.

All over the world a good amount of business of herbal medicines is done and the handsome revenue earned from it which leads to coming of poor quality, or adulterated herbal medicines in international markets. These poor quality or adulterated herbal medicines raise a serious issue of patient safety. The complex nature and lack of standardization of herbal drugs make difficult to perform safety, quality and effectiveness tests of these medicines. The quality of source materials containing a number of active ingredients and how properly, these are handled during process of manufacturing effects quality, safety, and efficacy of herbal medicine products. As the herbal medicines are natural or traditional it is a strong belief that they are safe. However, It has been proved on the bases of scientific evidences that if herbal medicines if taken in combination with other medicines, or in a wrong way and if they are of poor quality can cause harmful and adverse effects. Patient health and safety can be enhanced by increasing patient awareness about safe usage of herbal medicines, using quality raw materials in manufacturing, and strict quality control and its enforcement. (4)

The laws and regulations for herbal drugs are different in different countries. The National Regulatory Authority in India is the Central Drugs Standard Control Organization (CDSCO). Its equivalent counterparts elsewhere include Health Canada, the European Medicines Agency and the United States Food and Drug Administration (US FDA). CDSCO is an arm of the Ministry of Health and Family Welfare, Government of India. The mission of all these agencies is to safeguard and enhance public health by assuring the safety, efficacy and quality of drugs, cosmetics and medical devices [4]. WHO states that each country should have a system to regulate herbal drugs in their territory. These regulatory systems which are made by any country should ensure the efficacy, quality and safety of herbal medicines. During the framework of regulations for herbal drugs, the WHO guidelines should be considered by the countries. (5)

The WHO guidelines for herbal medicines guide the countries in the site selection for cultivation, collection procedures, plant identification and their differentiation from adulterants etc. (6) The WHO guidelines also help in post-harvest operations such as legal and labeling components which are come under the national and regional regulations on benefit sharing, patent status and quality standards. Although it is not mandatory for any country to follow WHO guidelines, but it's only a system or a framework which helps countries in framing of guidelines for the regulation of herbal drugs. The IUPAC subcommittee on bio molecular chemistry has also published protocols on efficacy, safety, documentation and standardization of herbal medicines. (7)

Challenges in Clinical Trials of Herbal Drugs

The active and control groups of herbal drugs are very difficult or sometimes impossible to get with identical smell, taste and color. The same problem may also come during the manufacturing of placebo which may exhibit specific distinguished taste and a strong aroma, these problems have small chances to overcome.

As many herbal systems have an integrated approach which cannot differentiate the patients with different diseases. This is becoming a

major problem during the inclusion and exclusion patients in clinical trials.

1. The outcomes of study of herbal drug which is administered to a group of subjects of different make ups may not be uniform.
2. At different stages of disease traditional treatment systems may include different interventions in the same patient, which can cause variation in a clinical trial.
3. In case of herbal drugs, clinical trial the attainment of statistical significance is a very difficult task because of insufficient numbers of patients.
4. Randomized clinical trials are not possible in the case of herbal drugs because different result may come with the same patients which make the selection process more difficult.
5. Herbal drugs used in clinical trials are not standardized and not of appropriate quality. (1)

The use of most recent guidelines and methodologies of clinical trials can overcome these challenges. During the manufacturing of herbal drugs masking of strong aroma and fine coating blinds the typical colors can be done by using modern manufacturing techniques, and WHO approved, ISO certified units. This makes easy to perform blinding methods for clinical trials. Planning of scientific, clinical study design is very much essential for success of any clinical trial which is applicable here. To obtain reliable clinical trial results for herbal medicines, double-blind experiments should be applied with enough patients selected, ideally using the standard of clinical trial for new drug development. (8)

Ethical Considerations in Clinical Trials with Herbal Products

During the process of clinical research on herbal medicine, fundamental ethical principles should be followed to include humans as a subject of research. Before starting research risks and benefits must be assessed and research must be benefited to the participant, selection of subject must be reasonable, design of research must be sound and Consent of the subject must be obtained from the subject or its legal representative.

Some important points that should be considered in the clinical trials process of herbal products:

- The Product must be of good quality and must not be adulterated.
- Herbal product interactions with other chemical entities and food.
- Product organ toxicity data must be gathered
- The Prior dose must be found before the experiment is done in humans.

During the informed consent process the uncertainty of these points must be clearly stated to the subjects. The clinical trials of herbal drugs may give biased results which can be minimized by giving more attention to study design including appropriate control groups. It will be beneficial for both the community from whom drug originates and the researcher. when the benefits and results of research will be shared with this community. Patient safety in clinical research is assured if the research is performed by well-trained ethical investigator. Therefore, experienced and skillful clinicians as investigators should assure quick recognition and appropriate management of any experiential adverse effects or getting worse of a condition which is exist before starting of clinical research. Same vigilant attitude must be followed by ethical committees for herbal research as they do for conventional treatment protocols. (9)

European Regulations and Guidelines

Herbal medicinal products, marketing authorization granted under the European Directive 2001/83/EC on the basis of quality, safety and efficacy tests and experimentations results. Definition traditional herbal medicine, provisions for a community list of herbal substances and community herbal monographs and simplified registration procedure are the main features of Directive 2001/83/EC. The Committee on Herbal Medicinal Products (HMPC) which is part of the EMA was

established under regulation (EC) No 726/2004 and European Directive 2004/24/EC in September 2004. European Directive 2004/24/EC simplifies the registration procedure for herbal drugs as many companies face a lot of difficulties in fulfilling the requirements of Directive 2001/83/EC particularly in relation to efficacy of traditional herbal medicinal products. The evaluation of medicinal products, simplification of registration, authorization of herbal medicinal products, establishment of list of herbal substances and preparations and Community herbal monographs are some important tasks performed by the HMPC. The quality requirements for herbal substances and products are provided in HMPC Monographs of European Pharmacopoeia. Various qualities, non-clinical, clinical efficacy and safety issues has also addressed in several HMPC guidance documents. It is the responsibility of HMPC to identify the priority herbal constituents/ products/combinations and they should be covered by a monograph or a list entry. (10) Under the directive 2004/24/EC the herbal medicinal product, herbal drug substances and herbal preparations are described as follows:

Herbal Substances

An unprocessed usually dried form and sometimes fresh whole plants, plant parts, cut plants, fungi, algae, lichen and certain exudates of plants are considered to be herbal substances. Herbal substances are identification and recognition is done by their plant part used and their botanical name based on the binomial system (genus, species, variety and author).

Herbal Preparations

Herbal substances are subjected to various process such as extraction, expression, distillation, fractionation, purification, concentration or fermentation to convert into herbal preparations i.e. extracts, essential oils, expressed juices, powdered herbal substances, tinctures and processed exudates. Herbal Medicinal products are marketed in following three categories:

1. A traditional herbal medicinal product having sufficient safety data and plausible efficacy and a Member State granted a traditional use registration (simplified registration procedure) to this product.

2. An herbal medicinal product can be marketed under entrenched therapeutic use requirements (all around established use). This is exhibited with adequate safety and efficacy data. Accordingly the herbal product is allowed a marketing approval generally by a Member State or by the European Medicines Agency under specific conditions. (While approval from both have particular necessities, both administrative ways include the evaluation of general bibliographic safety and efficacy data, which are typically joined, for safe use of herbal products, with product particular information)

3. An herbal product can be approved after assessment of a marketing authorization application comprising of just “particular safety and efficacy data of product” (full dossier). Subsequently the herbal medicinal product is allowed a marketing authorization by the Agency or a Member State by means of the centralized procedure on the off chance that all necessities are met. (11)

Regulations

Member states of European Union give marketing approval to most of the herbal medicinal products separately, the information regarding the products and its approval is harmonized all around the European Union. The Committee on Herbal Medicinal Products (HMPC) prepared community herbal monographs is significant for the well-established use marketing authorization as well as the traditional use registration. The Committee on Herbal Medicinal Products (HMPC) prepares community herbal monograph scientifically on the bases of safety and efficacy data of an herbal substance and its products proposed for therapeutic use. In addition to non-clinical and clinical data the HMPC also documents all assessments scientifically done on the existing long-lasting use and experience of herbal products in the Community. Community monographs are partitioned into two segments: traditional use (simplified registration) and well-

established use (marketing authorization). The Traditional use segment is prepared on the basis of adequate safety data and probable efficacy while the well-established use segment refers to the safety and efficacy data. A traditional use registration applicant or a marketing authorization applicant can use final community monograph as an application reference material. The competent authorities and applicants in the Member States legally adhare to the Community list of herbal substances, preparations and combinations and the Community herbal monographs as:

- If applicant proves that the proposed herbal medicinal product and associated statements in the application meet the terms given in the community list it is not a mandate for him to make available proofs of the harmless and traditional use of a herbal medicinal product for which he looks forward for a traditional use registration.

- Competent authorities do not have the power to ask for further data to evaluate the traditional use and the safety of the product. (12)

Through list entries the 'Community list' is gradually developed. After the Committee has entered an herbal substance or product in a draft list, for public consultation it is released on the committee website for a three month period. Before list entry is submitted for authorization to European Commission it is finalized scientifically by the Committee on Herbal Medicinal Products (HMPC). Following this authorization, community list is published by the European Commission. (12)

The document of list entry comprises of following information:

- The common name of herbal substance in all EU languages and its scientific/botanical name.

- The indication (use of herbal substance).

- The dose and specified strength of herbal substance.

- The dosage form and route of administration and.

- Any other information such as contraindications, warnings and precautions required for the herbal substance or preparation can be used safely as a constituent of a traditional herbal medicinal product.

On the website of EMEA the procedure, SOPs, format and template have been made available for revision and preparation of community list entries and community monographs. The procedure of receiving scientific information, data on herbal substances and products from the community has been made by the Committee on Herbal Medicinal Products (HMPC). During the Community list entries and the Community monographs development process this provided information may be used by the Committee. After the 2-month period following the publication date in reply to a request for the submission of scientific data 'Scientific supporting information' can be sent to the committee in paper format (two copies via post or fax) or electronic format (e-mail or CD-ROM). On the EMEA website under preparation monographs and finalized community monographs both have been made available by the HMPC.

A binding Community mechanism has been formed by the Community pharmaceutical regulation which may be beckoned in supposing referrals. These referrals lead to a supposition from which the Commission issues a solitary choice tended to all Member States which is accounted for data to the applicants or marketing authorization holders. Notwithstanding these referrals as indicated by Articles 29, 30, 31, and 35 and 36 of Directive 2001/83/EC, Community pharmaceutical regulation has additionally made a method by which Member States may make reference to certain matters of THMP to the HMPC of the Agency, however which does not require Community method. These conditions are expected in:

1. Article 16c (1)(c) of Directive 2001/83/EC ("Adequacy of evidence of the long standing use referral");

2. Article 16c (4) of Directive 2001/83/EC ("Traditional use less than 15 years referral").

These referrals to the HMPC lead to a sentiment furthermore now and again the Article 16c (4) referrals may prompt a monograph which Member States might check. (13)

Regulations: of Herbal Drug in United States of America

Herbs are classified as dietary supplements by the Dietary Supplement Health and Education Act (DSHEA) of 1994 in the US. This law defines supplements quite broadly as "anything that supplements the diet." Supplements therefore include vitamins, minerals, herbs, amino acids, enzymes, organ tissues, metabolites, extracts, or concentrates. A major difference between a drug and a dietary supplement is that dietary supplements may not claim to "diagnose, cure, mitigate, treat, or prevent illness." It is interesting to note that dietary supplement manufacturers are allowed to make certain "structure/function" claims, which are often vaguely worded claims of health benefits. For example, an Echinacea product (often used to treat or prevent the common cold) might claim to "support the body's natural defences."

Dietary supplements can be produced, sold, and marketed without first demonstrating safety and efficacy, as is required for pharmaceutical drugs. Also, the FDA bears the regulatory burden of proving that a dietary supplement is unsafe before it can be removed from the market—which is in direct contrast to drugs, where a manufacturer must provide the FDA with evidence of safety and efficacy before a product can be sold. (14)

Not surprisingly, this regulatory structure has led to problems with the consistency and safety of herbal products. Several recent studies have documented dramatically different levels of suspected active ingredients in herbal products. For example, a recent analysis of 25 available ginseng products found a 15to 200 fold variation in the concentration of 2 ingredients believed to have biological activity: Ginsenosides and Eleuthrosides. Therefore, it may be difficult for patients to ascertain with certainty the precise contents of the products they may be interested in taking. (15)

In the United States, for traditional medicine systems such as using acupuncture in addition to usual care to help lessen pain, the term 'complementary/alternative medicines' (CAM) is generally used. Most utilization of CAM by Americans is corresponding (National Center for Complementary and Alternative Medicine (http://nccam.nih.gov). In place of conventional medicine, CAM uses 'Alternative medicine'. An exercise that associated both conventional and CAM therapeutic managements for which there is proof of effectiveness and safety uses term "Integrative medicine" (also called integrated medicine). CAM procedures are categorized into broad categories, such as manipulative and body-based practices, mind-body medicine and natural products. These categories are useful to talk over the CAM procedures, even these are not well-defined. Some of the CAM procedures may fall into more than one category. The term CAM can also be used for practice of traditional healers. Traditional healers passed from one generation to another generation use ways and means based on beliefs, experiences and indigenous theories. (16)

The USFDA categories the Complimentary Alternative Medicines (CAM) products into new drug and new animal drug, cosmetic, dietary supplement, food/food additive and devices in its draft guidance "Guidance for industry on complementary and alternative medicine products". Some CAM products are covered by these statutory definitions. It was additionally illuminated that CAM products were not exempted by the FDA Act and the Public Health Service Act from regulation. After recommendations of the American Herbal Products Association (AHPA) the draft guideline was later withdrawn.

Herbal Drug Products are differentiated in two categories first is those marketed as Over-The-Counter (OTC) and second is those require New Drug Application (NDA) by guidance for herbal drug products given by FDA's Center for Drug Evaluation and Research (CDER). Herbal drugs of well-known history of use and people not demands for certain information from them the

guidance document provides new drug route navigation such as discussions of the possibility of lesser demand for information by the public. FDA may consider toxicology studies or associating studies related waiver on a case to case basis. Under IND to support an initial clinical trial a waiver is entitled to new herbal drugs on the basis of preclinical pharmacology/toxicology studies, depending on earlier human experience. Except those herbal drug products regulated under section 351 of the Public Health Service Act (42 U.S.C. 262), all herbal drug products that are regulated under the act addressed by this guidance. (17)

Herbal products containing plant material as ingredients are called finished or labeled products. In the United States herbal drug products may be marketed under an approved NDA or ANDA or an OTC drug monograph. The FDA regulation 21 CFR parts 331-358 stated if an herbal product has been marketed for a long period of time for a specific OTC drug indication may be eligible for inclusion in an OTC drug monograph. If the manufacturer wants to amend the monograph for inclusion of an herbal substance as a new active constituent must submit a petition in accordance with 21 CFR 10.30.

Any person, after publishing the final OTC drug monograph of an herbal drug product for a specific indication, may market that product even it contains the same ingredient and for the same indication, but the only condition is that he should provide the labeling and other active ingredients (if present) according to all relevant monographs and other applicable regulations. The USFDA gives 5 years of market exclusivity from the time of approval to the drug developer for new drug entity if it has been approved under an NDA even in the absence of patent protection. A new herbal drug contains a number of chemical constituents may be eligible as a new chemical compound under § 314.108(a). During the period of exclusivity of herbal drug product if any other manufacturer got success in qualification his product as a new chemical entity for the same indication, the FDA won't approve it, or in a number of cases even review, unless the second manufacturer submits a 505(b) (1) application and performs all studies required to prove the safety and effectiveness of its product. Therefore, the manufacture should seek approval of an NDA after proving the safety and effectiveness of his product rather than request the competent authority to amend a monograph if he has desire to market his herbal drug product which is not included in the current OTC drug monograph. In addition a document that contains a schematic presentation of various regulatory approaches such as an OTC drug monograph and NDA procedures can help in marketing herbal drug products in the United States. To ensure a high degree of safety and effectiveness of herbal products and quality control standards during the manufacturing of herbal supplements and medicines, AHPA published GACP (Good Agriculture and Collection Practices) guideline in the American Herbal Pharmacopoeia. It is becoming easier for researchers to incorporate evidence based medicines and traditional understanding by using modern analytical techniques and standardization of herbal drug products. Herbal drug product safety and quality issues can be reduced by integration of evidence based medicines and traditional understanding. (18)

Indian Regulation

In India all the officially recognized health systems *viz. Ayurveda, Siddha, Yoga,* Homeopathy, Unani and Naturopathy except Allopathy have major share of herbal drug products. In India herbal drugs are regulated by Research Councils (ICMR and CSIR) Department of AYUSH (*Ayurveda, Yoga* & Naturopathy, *Unani, Siddha* and Homoeopathy), Drugs and Cosmetics Act 1940 (Amendment) and IMCC (Central Council of Indian Medicine) Act. Drug Controller General of India (DCGI's) regulations must be followed in case of herbal medicinal plants and remedies required to be incorporated into modern system.

According to the 1964 amendment of Drugs and Cosmetics Act 1940, all "*Ayurvedic, Siddha* or *Unani*" medicines specified in the Schedule First those are proposed for the diagnosis, prevention and treatment of disease in human beings or animals and developed under the procedures described in the books of *Ayurvedic, Siddha* and *Unani* systems of health. Some degree of controls provided by the 1964

amendment, for example, over manufacturing of drug which is performed by a qualified person under given hygienic conditions using unadulterated raw materials and all ingredients are labeled properly. The Ministry of Health and Family Welfare (Department of Health) established Pharmacopoeial Laboratory for Indian Medicine (PLIM) in Ghaziabad to overwhelm the difficulty comes in implementation of the 1964 amendment of the FD&C Act. PLIM comprises of the Drug Depot, the Drug Standardization and Testing Unit and the Herbarium and Reference Museum. Indian systems of health were also described in Pharmacopoeias. (12)

In India there is a provision to register herbal medicinal products in each state via state drug licensing authority. Recently Schedule TA (Rules 2008) has been introduced in the Drugs and Cosmetics Act (first amendment) for utilization of record of raw materials by licensed manufacturing units of Ayurvedic or Sidha or Unani medicines or products. By the second amendment (Drugs and Cosmetics Rules 2008) manufacturer of herbal drug products can use excipients mention in Indian Pharmacopoeia or Prevention of Food Adulteration Act 1954 or Bureau of Indian Standards Act 1986.

The ICMR has also published GCP guidelines for traditional herbal drugs. These GCP guidelines have classified traditional herbal medicines into three groups (19):

1. Traditional Herbal drugs manufactured on the basis of study of regular use, Classical text and prescribed pharmacopoeia.
2. Traditional herbal formulations manufactured by new process in new combination using new plant based chemical entity for a new indication and toxicity data have been generated for acute, sub-acute and chronic toxicity.
3. Traditional herbal formulations based on GMP compliant Standardization. (20).

To develop safe, effective AYUSH products for a recognized disease organization such as ICMR, CSIR and Department of AYUSH work together.

Objectives of Department of AYUSH are:

- To control drug quality
- To establish pharmacopoeial standards
- Supervising functioning of Pharmacopoeial Laboratory of Indian Medicines (PLIM)
- Make interaction with the Quality Council of India (QCI)
- Supervising working of Indian Medicine Pharmaceutical Company Limited (IMPCL)
- AYUSH also works for implementation of Good Manufacturing Practices (GMP)

Digitalization of information & texts of traditional herbal medicinal formulations and promotion of local health traditions has been started by the AYUSH department with the introduction of IPR regime. Data related to Indian Systems of Medicine such as traditional information about herbal drugs has been provided on the Traditional Knowledge Digital Library (TKDL) (http://www.tkdl.res.in). Data from the texts of Indian medicine systems has been given in TKDL for more than 2.23 lakh formulations. TKDL is generated by the mutual dealings of Ministry of Health and Family Welfare, Ministry of Science and Technology, Department of AYUSH and Council of Scientific and Industrial Research (CSIR). TKDL inhibit fly-by-night inventors from getting patent on existing traditional knowledge and gives legality to such traditional systems. (20)

A certification scheme for AYUSH drug products has been introduced by the AYUSH department with the suggestion of QCI in 2009. The quality concerns such as safety, efficacy and quality of AYUSH products raised all the time. A new scheme of voluntary certification has been introduced with collaboration QCI to meet quality concerns of AYUSH products.

At present two types of Ayush certificates (Ayush Standard Mark and Ayush Premium Mark) are awarded to the herbal drug's manufacturer. Ayush Standard Mark awarded on the basis of compliance to local regulatory requirements. Ayush Premium Mark awarded

on the basis of the following options; Option A: fulfilment of WHO Guidelines based GMP Requirements and impurity level described in document of Certification Criteria. Option B: fulfilment of any importing country regulatory requirements. The ISO/IEC Guide 65, by NABCB and recommendation by QCI should be followed by CBs during the process of providing certificates for the above mentioned. The certified bodies, Bureau Veritas Certification (India) Pvt Ltd located at Mumbai and Foodcert India (P) Ltd located at Hyderabad has been approved under the scheme.

In recent times the Department of AYUSH introduced a number of regulatory guidelines regarding quality enhancement of herbal preparations. An assistance has been taken from the WHO guidelines on Good Agriculture and Field Collection Practices (GACPs) and Good Agricultural Practices made by the GLOBALGAP Secretariat during the preparation of specific guidelines on Good Agriculture Practices (GAPs) by the National Medicinal Plants Board (NMPB) an agency of the Department of AYUSH in India. These Good Field Collection Practices help to meet the standard made for different aspects of harvesting and post-harvest management of medicinal plants. (21) Herbal drugs regulations and related committees are described in table 1.

Table 1: Legislative framework for herbal drugs in EU, US &India (9, 14, 19).

Items	EU	US	India
Legislation	• CD 2001/83 ("basic" regulation) • CD 2003/63 of 25 June 2003 (Annex I, criteria) • CD 2004/24 (Traditional herbal medicinal products) • CD 2004/27 of 31 March 2004 (HMPC)	• The Dietary Supplement Health and Education Act (DSHEA) of 1994) • The FDA regulation 21 CFR parts 331-358 • The Public Health Service Act (42 U.S.C. 262)	• The Drugs and Cosmetics Act 1940 amended 1964. • The Drugs and Cosmetics Rules 2008. • The Prevention of Food Adulteration Act 1954 • The Bureau of Indian Standards Act 1986.
Committee	• Central European Authority with specified tasks. • Committees and Working Parties • Herbal Medicinal Products Committee – HMPC • Monographs and List Working Party - MLWP	• Center for Drug Evaluation and Research (CDER). • National Center for Complementary and Alternative Medicine	• Research Councils (ICMR and CSIR) • Department of AYUSH

CONCLUSION

A large part of the world population using the herbal medicines which might be a good source to earn money for the pharmaceutical companies of EU, US and India. But lacking of separate guidelines for herbal drug approval and complex nature of the existing regulatory framework of these countries restricts the growth of the herbal drug market. Currently it is very difficult and costly to go through the all regulatory requirements such as clinical research for the pharmaceutical companies. Thus, regulatory authorities of EU, US and India should simplify herbal regulation and give clinical assistance and incentives for the clinical research to herbal drug manufacturers.

ACKNOWLEDGEMENTS

The authors are highly thankful to the de the department of pharmaceutical sciences and the library of Maharshi Dayanand University where we have sought the references of the article.

CONFILCTS OF INTEREST

The authors declare that there are no conflicts of interest.

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